

,908,858

137

· Nuclear Magnetic Resonance Spectrum (270 MHz, CDCl₃) δ ppm:

7.74 (2H, doublet, J=9 Hz);
7.24 (2H, doublet, J=9 Hz);
7.21 (2H, doublet, J=9 Hz);
6.98 (2H, doublet, J=9 Hz);
6.73 (1H, singlet);
6.40 (1H, singlet);
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4.76 (2H, singlet);
3.50 (1H, singlet);
2.17 (3H, singlet).
Mass spectrum (EI) m/z 344 [M⁺].

EXAMPLE 130

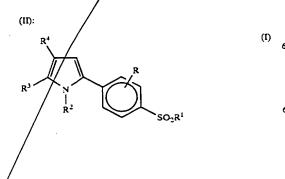
1-(4-Acetylthiophenyl)-4-methyl-2-(4sulfamoylphenyl)pyrrole (Compound No. 1-157)

0.90 g (2.6 mmol) of 1-(4-mercaptophenyl)-4-methyl-2-(4-sulfamoylphenyl)-pyrrole (prepared as described in Example 129) was dissolved in 15 ml of tetrahydrofuran, and 0.27 ml (2.9 mmol) of acetic anhydride was added to the 25 resulting solution. 0.53 ml (6.5 mmol) of pyridine was then added to the mixture, which was then stirred at room temperature overnight. The reaction mixture was then concentrated by evaporation under reduced pressure, and a saturated aqueous solution of sodium hydrogencarbonate 30 was added to the residue. The resulting mixture was then extracted with ethyl acetate. The organic extract was washed with water and dried over anhydrous magnesium sulfate, after which it was concentrated by evaporation under reduced pressure. The residue thus obtained was applied to 35 a silica gel chromatography column and eluted with a 3:2 by volume mixture of hexane and ethyl acetate, to give 0.44 g (yield 43%) of the title compound as a white powder, melting at 149-152° C.

Nuclear Magnetic Resonance Spectrum (270 MHz, CDCl₃) δ ppm:

7.75 (2H, doublet, J=9 Hz);
7.38 (2H, doublet, J=9 Hz);
7.22 (2H, doublet, J=9 Hz);
7.16 (2H, doublet, J=9 Hz);
6.80 (1H, singlet);
6.41 (1H, singlet);
4.78 (2H, singlet);
2.44 (3H, singlet);
2.18 (3H, singlet).
Mass spectrum (FAB) m/z: 386 [M*].
We claim:
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1. A compound of formula (I) or



Sp. /

15 wherein:

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R represents a hydrogen atom, a halogen atom or an alkyl group having from 1 to 6 carbon atoms;

R1 represents an alkyl group having from 1 to 6 carbon atoms an amino group or a group of formula -NHRª where Re represents an alkanoyl group having from 1 to 25 carbon atoms, an alkoxycarbonyl group having from 1 to 6 carbon atoms in the alkoxy part, an aralkyloxycarbonyl group in which the aralkyl part is as defined below, an alkanoyloxymethyl group having from 1 to 6 carbon atoms in the alkanoyl part, an alkoxycatbonyloxymethyl group having from 1 to 6 carbon atoms in the alkoxy part or a (2-oxo-1,3dioxolen-4-yl)methyl group which is unsubstituted or substituted at the 5-dioxolen position by an alkyl group having from 1 to 6 carbon atoms or by an aryl group as 30 defined below

R² represents a phenyl group which is unsubstituted or is substituted by at least one substituent selected from the group consisting of substituents α and substituents β

35 defined beldw;

R³ represents a hydrogen atom, a halogen atom or an alkyl group which has from 1 to 6 carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms;

R4 represents a hydrogen atom; an alkyl group which has from 1 to 6 carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms; a cycloalkyl group having from 3 to 8 carbon atoms, an aryl group which is as defined below, or an aralkyl group which is as defined below;

said aryl group having from 6 to 14 ring carbon atoms in a carbocyclic ring and are unsubstituted or are substituted by at least one substituent selected from the group consisting of substituents \alpha and substituents \beta, defined below;

said aralkyl group and the aralkyl part of said aralkyloxycarbonyl group are an alkyl group having from 1 to 6 carbon atoms and which are substituted by at least one

aryl group as defined above;

said substituents a are selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms; said substituents β are selected from the group consisting of an alkyl group which has from 1 to 6 carbon atoms and which is or

unsubstituted or are substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkythio group having from 1 to 6 carbon atoms; a mercapto group; an alkanoylthio group having from 1 to 6 carbon atoms; a mercapto group; an alkanoylthio group having from 1 to 6 carbon atoms; an alkylsulfinyl group having from 1 to 6 carbon atoms; a cycloalkyloxy group having from 3 to 8 carbon atoms; a haloakoxy group having from 1 to 6 carbon atoms; and an alkylenedioxy group having from 1 to 6 carbon atoms; and an alkylenedioxy group having from 1 to 6 carbon atoms;

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein R represents a hydrogen atom, a halogen atom or an alkyl group having 15 from 1 to 4 carbon atoms.

3. The compound of claim 1, wherein R represents a hydrogen atom, a thiorine atom, a chlorine atom or a methyl group.

4. The compound of claim 1, wherein R represents a 20 hydrogen arom.

5. The compound of claim 1, wherein R¹ represents a methyl group an amino group for an acetylamino group.

6. The compound of claim 1, wherein R¹ represents an amino group or in acetylamino group.

7. The compound of claim 1, wherein R² represents a phenyl group of a phenyl group which is substituted by at least one substituent selected from the group consisting of

a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 30 carbon atoms;

an unsubstituted alkyl group having from 1 to 4 carbon atoms; an alkyl group which has from 1 to 4 carbon atoms and which is substituted by at least one substituent selected from the group consisting of a halogen 35 atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms; a mercapto group; an alkanoylthio group having from 1 to 4 carbon atoms; a haloalkoxy group having from 1 to 4 carbon atoms and an alkylenedioxy group 40 having from 1 to 4 carbon atoms and an alkylenedioxy group 40 having from 1 to 4 carbon atoms.

8. The compound of claim 1, wherein R² represents a phenyl group or a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon 45 atoms, an alkylthio group having from 1 to 4 carbon atoms, an alkyl group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a mercapto group, an alkanoylthio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and an 50 alkylenedioxy group having from 1 to 4 carbon atoms.

9. The compound of claim 1, wherein R³ represents a hydrogen atom, a halogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms or a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having from 1 to 4 carbon atoms.

10. The compound of claim 1, wherein R³ represents a hydrogen atom, a halogen atom, an alkyl group having from 60 1 to 4 carbon atoms or a haloalkyl group having from 1 to 4 carbon atoms.

11. The compound of claim 1, wherein R⁴ represents a hydrogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms; a substituted alkyl group having from 1 65 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a

or

halogen atom, an alkoxy group having from 1 to 6 carbon

atoms and an alkylthio group having from 1 to 6 carbon atoms; a cycloalkyl group having from 3 to 6 carbon atoms; an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having from 1 to 4 carbon atoms, an unsubstituted alkyl group having from 1 to 6 carbon atoms, an alkyl group having from 1 to 6 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy having from 1 t/o 6 carbon atoms, and an alkylthio group having from 1 to 6 carbon atoms; a cycloalkyloxy group having from 3 to 8 carbon atoms; and an aralkyl group having from 1 to Acarbon atoms in the alkyl part and containing at least bee aryl group as defined in claim 1.

12. The compound of claim 1, wherein R4 represents a hydrogen atom; an unsubstituted alkyl group having from 1 to 4 carbon atoms; a substituted alkyl group having from 1 20 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom and an alkoxy group having from 1 to 6 carbon atoms; a cycloalkyl group having from 3 to 6 carbon atoms; an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms, an alkyl group having from 1 to 6 carbon atoms and which is unsubstituted or substituted by at least 30 one halogen atom and a cycloalkyloxy group having from 3 to 8 carbon atoms; and an aralkyl group having from 1 to 4 carbon atoms, in the alkyl part and containing at least one said aryl group.

13. The compound of claim 1, wherein:

R represents a hydrogen atom, a halogen atom or an alkyl group having from 1 to 4/carbon atoms;

R1 represents a methyl group Jan amino group for an

acetylamino grouff, R² represents an unsubstituted phenyl group or a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom: an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 4 carbon atoms; an alkyl group having from 1 to 4 carbon atoms which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1/to 4 carbon atoms and an alkylthio group having from/1 to 4 carbon atoms; a mercapto group; an alkanoy group having from 1 to 4 carbon atoms; a haloalky group having from 1 to 4 carbon atoms; and an alkylenedioxy group having from 1 to 4 carbon atoms;

R3 represents a Hydrogen atom, a halogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms or a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms;

R4 represents

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a hydrogen atom; an unsubstituted alkyl group having from 1 to 4 carbon

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from or

the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms:

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 6 carbon atoms; an alkylthio group having from 1 to 6 carbon atoms; an alkyl group having from 1 to 6 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having 1 to 4 carbon atoms and an alkylthio group having 1 to 4 carbon atoms; and a cycloalkoxy group having 3 to 8 carbon atoms; and an aralkyl group having from 1 to 4 carbon atoms; and an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group.

14. The compound of claim 1, wherein

R represents a hydrogen atom; a fluorine atom, a chlorine atom or a methyl group;

R1 represents an amino group or an acetylamino group

R² represents an unsubstituted phenyl group or a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having 1 to 4 carbon atoms, an alkyl group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a mercapto group, an alkanoylthio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and an alkylenedioxy group having from 1 to 4 carbon atoms and an alkylenedioxy group having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an alkyl group having from 1 to 4 carbon atoms or a haloalkyl group having from 1 to 4 carbon atoms;

R4 represents a hydrogen atom; an unsubstituted alkyl group having from 1 to 4 carbon atoms; a substituted alkyl group having from 1 to 4 carbon atoms and substituted by a least one substituent selected from the group consisting of a hydroxy group, a halogen atom and alkoxy group having from 1 to 6 carbon atoms; a cycloalkyl group having from 3 to 6 carbon atoms, an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at lest one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from A to 6 carbon atoms, an alkyl group having from 1 to 6 carbon atoms and which is unsubstituted or substituted by at least one halogen atom, and a cycloallyloxy group having from 3 to 8 carbon atoms; and an aralkyl group having from 1 to 4 carbon atoms 55 in the alkyl part and containing at least one said aryl group

15. The compound of claim 1, wherein:

R represents a hydrogen atom;

R1 represents an amind group or an acetylamino grouff;

R² represents an unsubstituted phenyl group or a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkyl group having from 1 to 4 carbon atoms, an alkyl group having from 1 to 4 carbon atoms, a

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haloalkyl group having from 1 to 4 carbon atoms, a mercapto group, an alkanoylthio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and an alkylenedioxy group having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an alkyl group having from 1 to 4 carbon atoms or a haloalkyl group having from 1 to 4 carbon atoms;

R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon atoms;

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom and an alkoxy group having from 1 to 6 carbon atoms;

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms, an alkyl group having from 1 to 6 carbon atoms and which is unsubstituted or substituted by at least one halogen atom, and a cycloalkyloxy group having from 3 to 8 carbon atoms; and

an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group.

16. The compound of claim 1, which is 4-methyl-2-(4-methylphenyl)-1-(4-sulfamoylphenyl)pyrrole.

17. The compound of claim 1, which is 2-(4-methoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl)pyrrole.

18. The compound of claim 1, which is 2-(4-

chlorophenyl)-4-methyl-1-(4-sulfamoylphenyl)pyrrole.

19. The compound of claim 1, which is 4-methyl-2-(4-methylthiophenyl)-1-(4-sulfamoylphenyl)pyrrole.

20. The compound of claim 1, which is 2-(4-ethoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl)pyrrole.

21. The compound of claim 1, which is 2-(4-methoxy-3-methylphedyl)-4-methyl-1-(4-sulfamoylphenyl)pyrrole.

22. The compound of claim 1, which is 2-(3-fluoro-4-methoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl)pyrrole.

23. The compound of claim 1, which is 2-(3,4-

dimethylphenyl)-4-methyl-1-(4-sulfamoylphenyl)pymole.

24. The compound of claim 1, which is 4-methyl-1-(4-

methylthiophenyl)-2-(4-sulfamoylphenyl)pyrrole.

[25. The compound of claim 1, which is 1-(4-acetylaminosilfonylphenyl)-4-methyl-2-(4-meth

methoxyphenyl) syrrole. [26. The compound of claim 1, which is 1-(4-acetylaminosulfonylphenyl)-4-methyl-2-(3,4-dimethylphenyl)pyrrole.

27. A method of treating or relieving pain or inflammation in a mammal suffering comprising administering to a mammal in need thereof an effective anti-inflammatory amount or effective analgesic amount of a compound selected from the group consisting of the compound of formula (I), the compound of formula (I), and a pharmaceutically acceptable salt of said compounds as claimed in claim 1.

28. The method of claim 27, wherein:

R represents a hydrogen atom, a halogen atom or an alkyl group having from 1 to 4 carbon atoms;

R1 represents a methyl grouf, 7 an amino group for an acetylamino grouf;

or

R2 represents an unsubstituted phenyl group or;

a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 5 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 4 carbon atoms; an alkyl group having from 1 to 4 carbon aloms and which is substituted by at least one substituent selected from the group consisting of a 10 halogen atom an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms; a mercapto group; an alkanoylthio group having from 1 to 4 carbon atoms; a haloalkoxy group having from 1 to 4 carbon atoms; and an alkylenedioxy group having from 1 to 4 carbon atoms;

R3 represents h hydrogen atom, a halogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms or a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms;

R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon 25

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group donsisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms 30 and an alkylthio group having from 1 to 6 carbon atoms:

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms 35 and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having 40 from 1 to 3 carbon atoms; an alkyl group having from 1 to 3 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms; and a cycloalkyloxy group having from 3 to 8 carbon atoms; and

an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group. 29. The method of claim 27, wherein:

R represents a hydrogen atom, a fluorine atom, a chlorine

atom or a methyl group;

R¹ represents an amino group or an acetylamino group, R² represents an unsubstituted phenyl group or a phenyl group which is substituted by at least one substituent 55 selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having from 1 to 4 carbon atoms, an unsubstituted alkyl group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon 60 atoms, a mercapto group, an alkanovithio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and an alkenedioxy group having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an alkyl 65 group having from 1 to 4 carbon atoms or a haloalkyl

group having from 1 to 4 carbon atoms;

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R4 represents

a hydrogen atom; an unsubstituted alkyl group haying from 1 to 4 carbon

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of/a hydroxy group, a halogen atom and an alkoxy group having from 1 to 6 carbon atoms:

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which/has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group; a halogen atom; an alkoxy group having from 1/to 6 carbon atoms; an alkyl group having from 1 to 6 carbon atoms and which is unsubstituted or substituted by at least one halogen atom; and a cycloalkyl group having from 3 to 8 carbon atoms; and an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group.

30. The method of claim 27, wherein said antiinflammatory and analgesic compound is selected from the group consisting of:

25 4-methyl-2-(4-methylphenyl)/1-(4-sulfamoylphenyl) pyrrole;

2-(4-methoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl) pyrrole;

2-(4-chlorophenyl)-4-mgthyl-1-(4-sulfamoylphenyl)

pyrrole;

4-methyl-2-(4-methylth/ophenyl)-1-(4-sulfamoylphenyl) pyrrole;

2-(4-ethoxypheny)//4-methyl-1-(4-sulfamoylphenyl) pyrrole;

35 2-(4-methoxy/3-methylphenyl)-4-methyl-1-(4sulfamoylphenyl)pymole; 2-(3-fluoro-4 methoxyphenyl)-4-methyl-1-(4-

sulfamoylphenyl)pyrrole;

2-(3,4-dimethylyhenyl)-4-methyl-1-(4-sulfamoylphenyl) pyrrole;

4-methyl-1-(4-methylthiophenyl)-2-(4-sulfamoylphenyl) pyrrole[;] [1-(4-acetyleminosulfonylphenyl)-4-methyl-2-(4-

methoxyphenyl)pyrrole; and

45 1-(4-acety/aminosulfonylphenyl)-4-methyl-2-(3,4dimethylphenyl)pyrrole.

31. A method of inhibiting bone resorption in a mammal comprising administering to a mammal in need thereof a pharmaceutically effective amount of a compound selected from the group coasisting of the compound of formula (I), the compound of formula (II), and a pharmaceutically acceptable sait of said compounds as claimed in claim 1. 32. The method of claim 31, wherein:

R represents a hydrogen atom, a halogen atom or an alkyl group having from 1 to 4 carbon atoms;

or R1 represents a methyl group an amino group or an acetylamind grouff;

and

R² represents

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an unsubstituted phenyl group or

a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom; \an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 4 carbon atoms; an alkyl group having from 1 to 4 carbon atoms and which is substituted by at least

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one substituent selected from the group consisting of a halogen atom, an alkoxy group having 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms; a mercapto group; an alkanoylthio group having from 1 to 4 carbon atoms; a haloalkoxy group having from 1 to 4 carbon atoms and an alkylenedioxy group having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms or a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms;

R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon atoms:

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms;

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 6 carbon atoms and an alkyl group having from 1 to 6 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms; and

an aralkyl group having from 1 to 4 carbon atoms in the alkyl pare and containing at least one said aryl group. 40

33. The method of claim 31, wherein:

R represents a hydrogen atom, a fluorine atom, a chlorine atom or a methyl group;

R¹ represents an amino group or an acetylamino group, R² represents an unsubstituted phenyl group or

a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a mercapto group, an alkanoylthio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and an alkenedioxy group 55 having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an alkyl group having from 1 to 4 carbon atoms or a haloalkyl

group having from 1 to 4 carbon atoms;

R⁴ represents a hydrogen atom, an unsubstituted alkyl 60 group having from 1 to 4 carbon atoms, a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom and an alkoxy group having from 1 to 6 carbon atoms, 65 a cycloalkyl group having from 3 to 6 carbon atoms, an aryl group which has from 6 to 10 ring carbon atoms

146 and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkyl group having from 1 to 6 carbon atoms and which is unsubstituted or substituted by at least one halogen atom, and a cycloalkyloxy group having from 3 to 8 carbon atoms, an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group. 34. The method of claim 31, wherein said active compound is selected from the group consisting of: 4-methyl-2-(4-methylphenyl)-1-4-suifamoylphenyl) 2-(4-methoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl) pyrrole; 2-(4-chlorophenyl)-4-me/hyl-1-(4-sulfamoylphenyl) pyrrole;

4-methyl-2-(4-methylth/ophenyl)-1-(4-sulfamoylphenyl)

pyπole; 2-(4-ethoxyphenyl)/4-methyl-1-(4-sulfamoylphenyl)

pyπole; 2-(4-methoxy-2-methylphenyl)-4-methyl-1-(4-

sulfamoylphenyl)pymole; 2-(3-fluoro-4/methoxyphenyl)-4-methyl-1-(4sulfamoylphenyl)pyrrole;

2-(3,4-dimeth/lphenyl)-4-methyl-1-(4-sulfamoylphenyl) pyrrole; -

4-methyl-1-(4-methylthiophenyl)-2-(4-sulfamoylphenyl) pyrrole;]

and

or

30 1-(4-acetylaminosulfonylphenyl)-4-methyl-2-(4methox/phenyl)pyrrole; and

1-(4-acetylaminosulfonylphenyl)-4-methyl-2-(3,4dimethylphenyl)pyrrole.

35. A method of inhibiting leukofriene production in a mammal comprising administering to a mammal in need thereof a compound selected from/the group consisting of the compound of formula (I), the compound of formula (II) and a pharmaceutically acceptable salt of said compound as claimed in claim 1.

36. The method of claim 33, wherein:

R represents a hydrogen atom, a halogen atom or an alkyl group having from 1 to 4 carbon atoms;

R2 represents a methyl group jan amino group for an acetylamino group;

R2 represents

an unsubstituted phenyl group or a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 4 carbon atoms; an alkyl group having from 1 to/4 carbon atoms and which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 karbon atoms; a mercapto group; an alkanoythio group having from 1 to 4 carbon atoms; a haloalkoxy group having from 1 to 4 carbon atoms; and an alkylenedfoxy group having from 1 to 4 carbon atoms:

R3 represents /a hydrogen atom, a halogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms or a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthro group having from 1 to 4 carbon atoms;

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R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon atoms;

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms.

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 6 carbon atoms; an alkyl group having from 1 to 6 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms; and a cycloalkyloxy group having from 3 to 8 carbon atoms; an aralkyl group having from 1 to 4 carbon atoms in the alkyl part 25 and containing at least one said aryl group.

37. The method of claim 35, wherein:

R represents a hydrogen atom, a fluorine atom, a chlorine atom or a methyl group;

R¹ represents an amino group or an acetylamino group; 30 R² represents

an unsubstituted phenyl group or

a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a mercapto group, an alkanoylthio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and a alkylenedioxy group having from 1 to 4 carbon atoms and a alkylenedioxy group having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an alkyl group having from 1 to 4 carbon atoms or a haloalkyl

group having from 1 to 4 carbon atoms;

R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon atoms;

a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group and an alkoxy group having from 1 to 6 carbon atoms;

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group; a halogen atom; an alkoxy group having from 1 to 6 carbon atoms; an unsubstituted alkyl 60 group having from 1 to 6 carbon atoms; an alkyl group having from 1 to 6 carbon atoms and which is unsubstituted or substituted by at least one halogen atom; and a cycloalkyloxy group having from 3 to 8 carbon atoms; and an aralkyl group having from 1 to 4 carbon 65 atoms in the alkyl part and containing at least one said aryl group.

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    38. The method of claim 35, wherein said active com-
  pound is selected from the group consisting of:
  4-methyl-2-(4-methylphenyl)-1-(A-sulfamoylphenyl)
     pyπole;
5 2-(4-methoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl)
     pyrrole;
  2-(4-chlorophenyl)-4-methyl-1-(4-sulfamoylphenyl)
     pyrrole;
   4-methyl-2-(4-methyl miophenyl)-1-(4-sulfamoylphenyl)
     pyrrole;
   2-(4-ethoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl)
     pyrrole;
                     -methylphenyl)-4-methyl-1-(4-
   2-(4-methoxy
sulfamoylpheffyllpyrole;
15 2-(3-fluoro-4-methoxyphenyl)-4-methyl-1-(4-
     sulfamoylphenyl)pyrrole;
   2-(3,4-dime/hylphenyl)-4-methyl-1-(4-sulfamoylphenyl)
                                                                                              and
     pyrrole;
   4-methyl-A-(4-methylthiophenyl)-2-(4-sulfamoylphenyl)
     pyrrole
  [1-(4-acetylaminosulfonylphenyl)-4-methyl-2-(4-
     methoxyphenyl)pyrrole; and
   1-(4-acetylaminosulfonylphenyl)-4-methyl-2-(3,4-
     dimethylphenyl)pyrrole.]
     39. A method of selectively inhibiting the activity of
   COX-2 in a mammal comprising administering to said mammal appearance trically effective amount of a com-
   pound selegion from the group consisting of the compound
   of formula (II), the compound of formula (II) and a pharma-
30 ceutically acceptable salt of said compounds as claimed in
   claim 1.
      40. The method of claim 39, wherein
      R represents a hydrogen atom, a halogen atom or an alkyl
        group having from 1 to 4 carbon atoms;
      R1 represents a methyl group an amino group or an
                                                                                          or
        acetylamino group;
      R2 represents
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an unsubstituted phenyl group or

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a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom; an alloxy group having 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 4 carbon atoms; an afkyl group having from 1 to 4 carbon atoms and which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms; a mercapto groups an alkanoylthio group having from 1 to 4 carbon atoms; a haloalkoxy group having from 1 to 4 carbon atoms; and an alkylenedioxy group having from 1 to 4 carbon atoms;

R3 represents a hydrogen atom, a halogen atom, an unsubstituted alkyl group having from 1 to 4 carbon atoms or a substituted alkyl group having from 1 to 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms and an alkylthio group having from 1 to 4 carbon atoms;

R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon

a substituted alkyl group having from 1 to 4 carbon atoms 65 and substituted by at least one substituent selected from

consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms;

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a halogen atom; an alkoxy group having from 1 to 4 carbon atoms; an alkylthio group having from 1 to 4 carbon atoms; an unsubstituted alkyl group having from 1 to 6 carbon atoms; an alkyl group having from 1 to 6 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, an alkoxy group having from 1 to 6 carbon atoms and an alkylthio group having from 1 to 6 carbon atoms; and a cycloalkyloxy group having from 3 to 8 carbon atoms; and

an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group.

41. The method of claim 39, wherein:

R represents a hydrogen atom, a fluorine atom, a chlorine atom or a methyl group;

R¹ represents an amino group or an acetylamino group; R² represents

an unsubstituted phenyl group or

a phenyl group which is substituted by at least one substituent selected from the group consisting of a halogen atom, an alkoxy group having from 1 to 4 carbon atoms, an alkylthio group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a haloalkyl group having from 1 to 4 carbon atoms, a mercapto group, an alkanoylthio group having from 1 to 4 carbon atoms, a haloalkoxy group having from 1 to 4 carbon atoms and a alkylenedioxy group having from 1 to 4 carbon atoms;

R³ represents a hydrogen atom, a halogen atom, an alkyl group having from 1 to 4 carbon atoms or a haloalkyl group having from 1 to 4 carbon atoms;

R4 represents

a hydrogen atom;

an unsubstituted alkyl group having from 1 to 4 carbon atoms;

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a substituted alkyl group having from 10 4 carbon atoms and substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom, and an alkoxy group having from 1 to 6 carbon atoms;

a cycloalkyl group having from 3 to 6 carbon atoms;

an aryl group which has from 6 to 10 ring carbon atoms and which is unsubstituted or is substituted by at least one substituent selected from the group consisting of a hydroxy group, a halogen atom; an alkoxy group having from 1 to 6 carbon atoms; an alkyl group having from 1 to 6 carbon atoms which is unsubstituted or substituted by at least one halogen atom; and cycloalkyloxy group having from 3 to 8 carbon atoms; and

an aralkyl group having from 1 to 4 carbon atoms in the alkyl part and containing at least one said aryl group.

42. The method of claim 39, wherein said active com-

pound is selected from the group consisting of: 4-methyl-2-(4-methylphenyl)-1-(4-sulfamoylphenyl)

4-methyl-2-(4-methylphenyl)-1-(4-sulfamoylphenyl

2-(4-methoxyphenyl)-4-methyl-1-(4-sulfamoylphenyl) pyrrole;

2-(4-chlorophenyl)-4-methyl-1-(4-sulfamoylphenyl)
pyrrole;

25 4-methyl-2-(4-methylthiophenyl)-1-(4-sulfamoylphenyl)
pyrrole;

2-(4-ethoxyphenyl) 4 methyl-1-(4-sulfamoylphenyl)
pyrrole;
2-(4-methoxy-)-methylphenyl)-4-methyl-1-(4-

sulfamoylphenyl)pymole; 2-(3-fluoro-4-methoxyphenyl)-4-methyl-1-(4-

suifamoylphenyl)pyrrole; 2-(3,4-dimethylphenyl)-4-methyl-1-(4-sulfamoylphenyl)

and

[1-(4-a octylaminosulfonylphenyl)-4-methyl-2-(4-methoxyphenyl)pyrrole; and

1-(4/acetylaminosulfonylphenyl)-4-methyl-2-(3,4-dimethylphenyl)pyriols.

dimethylphenyl)pyrrole.]
43. The compound of claim 8, wherein the phenyl group is substituted with 1 to 3 of said substitutents.

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